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Quantitative MRI to define mechanisms of CArDiovascular co-morbidity in patients with Early Rheumatoid Arthritis and to measure the effect of biological therapy

Submission date
08/11/2013

Recruitment status
No longer recruiting

Registration date
08/11/2013

Overall study status
Completed

Last Edited
23/10/2018

Condition category
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
In this study, we aim not only to measure the effects of arthritis treatment, including the effect of the drug etanercept, but also to look at the effect it has on the heart and blood vessels. This is important because, in long-term rheumatoid arthritis, there is an increased risk of heart disease and disorders of blood vessels, such as stroke. This study will use MRI scanning technique to provide an insight into heart disease in patients with rheumatoid arthritis and allow us to study the effects of early biologic treatment.

Who can participate?
Men and women, aged between 18 and 80 years, diagnosed with rheumatoid arthritis, who have not yet received a drug treatment and who have disease symptoms for less than 1 year can participate in this study. We also enroll men and women without rheumatoid arthritis, aged between 18 and 80 years for comparison.

What does the study involve?
All participants receive Magnetic Resonance Imaging (MRI) of the heart at the start of the study and then at end of year 1 and end of year 2. MRI is a widely used and safe technique for imaging soft tissues within the body. MRI can assess what the blood vessels look like and how well the heart functions. Up to 20 ml (approximately 2 tablespoons) of extra blood will be taken at three of the study visits. This will be tested in this sub-study, but it will also be stored (in an anonymised way, i.e. your identity will not be shown on the samples) for possible future research. Pulse Wave Velocity measurements are taken to find out how fast blood travels from one point in the body to the next. Blood travels faster if blood vessels are stiffer, and stiffer blood vessels suggest a higher risk of heart disease.

What are the possible benefits and risks of participating?
Patients may receive beneficial information about the disease. This study may help us to better treat patients in the future. No personal benefits will be gained directly by the patients.

Collection of blood may cause symptoms such as local pain, bleeding, bruising, fainting, and rarely infection. Magnetic Resonance Imaging (MRI) is safe and no radiation is used for this scan. There are no known risks from this technique. Some people may experience claustrophobia (discomfort of being in a closed space). Our MRI staff will do all that they can to make you feel comfortable during the scan, and will be monitoring you via a video camera and an audio link. If we are unable to make you feel comfortable in the scanner, we will not go ahead with scanning. The medication which we use is very safe but, as with any injection, reactions may occur. These include a warm sensation at the injection site, nausea or vomiting and skin rash. These effects usually only last for a few minutes. People with a history of allergy are more likely to suffer a more severe reaction, but this is rare (less than 1 in 3000). The department is equipped to cope with allergic reactions if they happen and medical staff will be on hand to deal with any unforeseen circumstances or problems. Adenosine, the medication we use to increase the blood flow to the heart, can cause flushing, breathlessness and chest discomfort. However, all of these feelings usually subside within one or two minutes or even more quickly if the medication is stopped

Where is the study run from?
The study is run from Chapel Allerton Hospital and The Leeds General Infirmary, both located in Leeds, UK.

When is the study starting and how long is it expected to run for?
The study started in July 2011 and expected to run until March 2016.

Who is funding the study?
The study is funded by the National Institute for Health Research (NIHR), UK.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2010-023910-30

Protocol serial number
15327

Study information

Scientific Title
Quantitative MRI to define mechanisms of cardiovascular co-morbidity in patients with early Rheumatoid Arthritis and to measure the effect of biological therapy: a randomised controlled trial

Acronym
CADERA

Study objectives
The main study hypothesis driving VEDERA and therefore CADERA is that early and untreated rheumatoid arthritis is fundamentally tumour necrosis factor-dominant, and therefore tumour necrosis factor inhibitor-responsive (TNFi) disease. Use of other non-biological disease modifying anti-rheumatic drugs (DMARDs) with delayed TNFi commencement alters the pro-inflammatory cytokine hierarchy to a more heterogeneous drive seen as more varied response to TNFi. Response to TNFi when started immediately is therefore postulated to be qualitatively and quantitatively superior.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leeds (West) Research Ethics Committee, 23/02/2011, 10/H1307/138 . Part of the overarching VEDERA study ethics approval (CADERA is the cardiovascular sub-study to VEDERA).

Study design
Randomised; Interventional; Design type: Screening

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Topic: Cardiovascular; Subtopic: Cardiovascular (all Subtopics); Disease: Atherothrombosis

Interventions
CADERA bolts on to the VEDERA trial, a prospective longitudinal intervention study of patients with early rheumatoid arthritis, randomized to either first-line anti-TNF therapy or optimal DMARD therapy. For the current proposal (CADERA), patients recruited to VEDERA will undergo cardiovascular MRI at baseline (prior to treatment) as well as after 1 year and 2 years of treatment. In order to determine that MRI can detect significant differences in cardiovascular

disease (CVD) in the study cohort, 30 controls matched to the first 30 VEDERA patients will be recruited and MRI findings between the two groups compared. The change in CVD status as defined by MRI between baseline and follow-up in patients treated with early biologics or optimal DMARD therapy will be determined. At the end of the study all patients will enter the IACON registry (a separate in-house observational trial).

Intervention Type
Other

Phase
Phase IV

Primary outcome(s)
The main outcome measures in this study are quantitative MRI measurements. Longitudinal changes of outcome measures in response to therapy will be measured and compared between the two treatment arms. Differences in outcome measures between the patient and control groups will be established.

1. Aortic distensibility

Key secondary outcome(s))
1. Left ventricle (LV) ejection fraction
2. LV strain and twist
3. Myocardial perfusion reserve

Completion date
31/01/2015

Eligibility

Key inclusion criteria
Patients:
1. Males and females
2. Aged between 18 and 80 years
3. Diagnosed with RA according to 2010 ACR/EULAR criteria
4. Who have not yet received therapy with disease modifying drugs
5. Have early (symptoms for less than 1 year)
6. Active disease (clinical or imaging evidence of synovitis and DAS28- ESR >/= 3.2)
7. At least one poor prognostic factor (anti-citrullinated peptide antibody +/- abnormal power Doppler in at least 1 joint)

Controls:
1. Males and females without RA
2. Aged between 18 and 80 years
3. Matched for age and blood pressure

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Patients:
1. Previous treatment with DMARDs
2. Contraindications to MRI and to anti-TNF therapy and severe co-morbidity that would in the clinicians opinion be associated with unacceptable risk of receiving potentially anti-TNF therapy
3. Contraindications to MRI (incompatible metallic implants, pacemakers)
4. Renal failure (eGFR<30 ml/min/1.73m2)
5. Previous allergic reactions to MRI contrast agents
6. Known cardiovascular disease (CVD)
7. Contraindications to adenosine (asthma or high grade heart block)

Controls:
1. History of RA or other inflammatory disease
2. Contraindications to MRI
3. Contrast agents or adenosine or presence of renal failure as defined above
4. Known CVD

Date of first enrolment
27/01/2012

Date of final enrolment
31/01/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Department of Rheumatology
Leeds
United Kingdom
LS7 4SA

Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (NIHR) - Efficacy and Mechanism Evaluation; Grant Codes: 11/117/27

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2017		Yes	No
Protocol article	protocol	08/11/2014		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes